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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040311

Application Number: 09/788,476
Filing Date: February 21, 2001
Appellant(s): CHUNG ET AL.

Mark J. Nuell
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10 December 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief contains a statement saying that there is no related appeals or interferences. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

Claims 15-17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

This appeal involves claim 1 as stated by the appellant in the brief.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Since claim 1 is appealed, grouping of claims are not applicable for the instant application.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claim under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is drawn to a genus of isolated nucleic acid molecules defined as having at least about 60% sequence identity and hybridizes under the recited high stringent conditions to the full length SEQ ID NO:1 or SEQ ID NO:3, wherein said nucleic acid molecules are differentially or preferentially expressed in human

hepatocellular carcinoma (HCC) or pancreatic adenocarcinoma as compared to normal control.

The specification discloses isolation of a human cDNA, SEQ ID NO:1 encoding SEQ ID NO:2 protein overexpressed in HCC and pancreatic adenocarcinoma. The specification also discloses a PCR product, SEQ ID NO:3 that encodes SEQ ID NO:2 protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity and hybridization. There is not even identification of any particular portion of the structure that must be conserved in order to have the recited function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that

[he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acid molecules, given that the specification has only described SEQ ID NO: 1 and 3. Therefore, only isolated nucleic acid comprising SEQ ID NO:1 and 3, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1 and 3, does not reasonably provide enablement for any other nucleic acid molecules having at least 60% identity to and also hybridizes to full SEQ ID NO:1 or 3 under conditions of 0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65 °C. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification discloses a human cDNA species SEQ ID NO:1 (termed as hcc-1) encoding SEQ ID NO:2 (HCC-1) protein. SEQ ID NO:3, a PCR product is a fragment of SEQ ID NO:1 that is used in expression of the SEQ ID NO:2 protein. The specification discloses that hcc-1 is overexpressed in HCC and pancreatic adenocarcinoma. It appears that it involves two steps to make the full scope of the claimed genus is: (1) to isolate other species by screening a large quantity of clinical samples, namely liver or pancreatic tissues from patients with HCC or pancreatic adenocarcinoma to determine what other mRNA species are differentially or

preferentially expressed in HCC or pancreatic adenocarcinoma; (2) to determine whether if the screened species meet the structural limitations of the instant claim. The (1) step above requires undue experimentation because the step involves screening a large quantity of clinical samples. In order to satisfy 35 U.S.C. 112, first paragraph, the specification should teach how to make the claimed invention, not how to screen it. In summary, the specification does not teach how to make a species having the recited function (i.e. differentially preferentially expressed in human HCC or pancreatic adenocarcinoma) and also having the recited structure (i.e. at least 60% identity to and also hybridizes to full SEQ ID NO:1 or 3 under conditions of 0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65 °C).

Considering the broad scope of the claims, and the limited teachings of the specification, it is concluded that undue experimentation would be required to enable the full scope of the claims.

(11) Response to Argument

WRITTEN DESCRIPTION

At pages 3 and 4, appellant cites MPEP 2163, University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407, and Example 9 of PTO Written Description Guidelines, Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609 as the applicable standard for the written description requirement.

At the paragraph bridging pages 3 and 4, appellant states that "the written description requirement for a claimed genus may be satisfied through sufficient description requirement of a representative number of species OR by disclosure or

relevant identifying characteristics, such as structure or other physical and/or chemical properties, OR by functional characteristics coupled with a known or disclosed correlation between function and structure".

The specification discloses a single cDNA species i.e. SEQ ID NO:1, which is differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in said subject and/or in subject not diagnosed with this condition. The specification discloses SEQ ID NO:3, which is a fragment of SEQ ID NO:1 that is inserted into a expression vector. The specification does not include an example, wherein either SEQ ID NO:1 or 3 is used under the recited highly stringent hybridization conditions (0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65 ^{o}C) for isolation of nucleic acids that are differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in said subject and/or in subject not diagnosed with this condition. The specification does not disclose the function of the claimed genus or the function of the protein(s) encoded by the claimed genus.

A review of the full content of the specification indicates the specification does not satisfy the first two alternative choices for written description requirement i.e. "discloses a representative number of species" or "disclosure or relevant identifying characteristics, such as structure or other physical and/or chemical properties".

The next analysis will be to determine whether the specification meets the written description requirement by describing functional characteristics coupled with a known or disclosed correlation between function and structure.

Appellant, at page 4 and pages 8-10, argues that the Examiner have overlooked that the claimed genus is hybridizable to the sequence under high stringency conditions. Appellant appears to argue that the instant claim 1 as currently construed is analogous to the hypothetical claim 1 of Example 9 in the USPTO Written Description Guidelines (the Guidelines).

Instant claim 1 reads:

> An isolated nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3 or a nucleotide sequence, having at least about 60 % similarity to the full length of SEQ ID NO:1 or SEQ ID NO:3, that hybridizes to SEQ ID NO:1 or SEQ ID NO:3 under conditions of 0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65 °C, wherein an mRNA corresponding to said nucleic acid is differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in said subject and/or in subject not diagnosed with this condition.

The hypothetical Claim 1 of Example 9 in the Guidelines reads:

> An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the compliment of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

In the hypothetical claim 1 of Example 9 in the Guidelines, the structure of the claimed genus encodes a protein with the recited function. In other words, the recited function is dictated by the chemical structure of the claimed genus.

However, unlike the situation in Example 9 of the Guidelines, the instantly recited function is not associated with the structural feature of claimed genera, but associated

with human disease status. In the instant claim 1, the recited function is not dictated by chemical structure of the claimed genus but dictated by other events i.e. that pancreatic adenocarcinoma or HCC is developed in a host. In other words, the expression is not function associated with the structure but a reaction of a human body to certain stimuli, in the instant case the development of HCC or pancreatic adenocarcinoma.

In summary, the functional characteristic recited is uncoupled with the structure of the claimed genus. There is no correlation between the chemical structure of the claimed genus and the recited function. Therefore the recited functional language describing the claimed genera does not adequately describe the common feature of claimed generic nucleic acid molecule.

Appellant at page 5 and 6 under the heading "EXTENSIVE EXPRESS DISCLOSURE" argues that the instant specification provides detailed and extensive disclosure relating to the sequence similarity determination and also argues that the present invention contemplates a method for the construction of a nucleic acid molecules comprising a non-naturally occurring nucleotide sequence for protein expression purposes and making such non-naturally occurring nucleotide is well known in the art. These arguments are drawn to limitation not present in the claim because the instant claim excludes a non-naturally occurring nucleotide. Instantly claimed invention is limited to naturally occurring nucleic acid molecules that are expressed in HCC or pancreatic adenocarcinoma.

SCOPE OF ENABLEMENT

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a genus of nucleic acid molecule with certain degree of similarity to SEQ ID NO: 1 or 3 that must be expressed in HCC or pancreatic adenocarinoma. The relative level of skill in the art in determining sequence similarity and in determining which nucleic acid molecules hybridizes to a given nucleic acid is high. However, the relative level of skill in isolating mRNA species that are differentially and preferentially expressed in HCC or pancreatic carcinoma is not high; this still requires screening a large quantity of clinical samples, namely liver or pancreatic tissues from patients with HCC or pancreatic adenocarcinoma; before isolating a species, one skilled in art has to determine what other mRNA species are differentially or preferentially expressed in HCC or pancreatic adenocarcinoma. In other words, the relative high level of skill in the art in determining sequence similarity and in determining which nucleic acid molecules hybridizes to a given nucleic acid is not applicable to predict which other similar sequence(s) to instant SEQ ID NO:1 or 3 is differentially or preferentially expressed in HCC or pancreatic adenocarcinoma. Which other similar

sequences could be used as HCC or pancreatic adenocarcinoma cancer marker is still unpredictable until said sequences are experimentally determined by screening a large quantity of appropriate clinical samples. The breadth of the claim is broad including unknown species. The level of predictability which nucleic acid molecule will be expressed in HCC or pancreatic adenocarcinoma is low. The amount of direction or guidance by the inventor how to make the full scope of claimed nucleic acid molecule with the recited structural element coupled with the recited function is limited. There are no working examples or guidance or direction to allow the person of ordinary skill in the art to make species in a manner commensurate in scope with the claims. The quantity of experimentation needed to make the invention is large. In order to make the full scope of the invention, one skilled in the art has to screen a large quantity of clinical samples from liver or pancreatic tissue of patients having HCC or pancreatic adenocarinoma, followed by sequence the nucleic acid composition.

At lines 6 from the bottom of page 6, Appellant states that the appellant and the examiner agrees that the relative level of skill in the art in determining sequence similarity and screen which nucleic acid molecules hybridizes to a given nucleic acid is high. At page 7 lines 1-6, appellant states that screening differentially or preferentially expressed mRNA is routine. At page 7 lines 7-19, appellant states that the specification discloses hcc-1 cDNA differentially or preferentially expressed in the tumors of interest. Appellant at bottom of page 7 argues "[t]he specification is looking for a **single** marker indicative of the specific tumors of interest". This argument is not persuasive because it is not commensurate in scope.

Instant claim 1 reads:

> An isolated nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3 or a nucleotide sequence, having at least about 60 % similarity to the full length of SEQ ID NO:1 or SEQ ID NO:3, that hybridizes to SEQ ID NO:1 or SEQ ID NO:3 under conditions of 0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65 °C, wherein an mRNA corresponding to said nucleic acid is differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in said subject and/or in subject not diagnosed with this condition.

The claim as currently construed is drawn to genus of markers (multiple species, not a single species), not a single marker.

Appellant at the paragraph bridging pages 7 and 8 argues "[i]n determining whether **an isolated nucleic acid** falls within the scope of claim 1" would be accomplished without undue experimentation given the high skill in the art in this area and the species determined to be fall within the structural requirement of the claim would likely have similar expression profile as SEQ ID NO:1 or SEQ ID NO:3. These arguments have been fully considered but found unpersuasive because one skilled in art cannot pick up **an isolated nucleic acid** from a coffee shop, or one's lab bench in order to determine whether it falls within the scope of claim 1.

Appellant missed a critical step i.e. how to isolate **an isolated nucleic acid**. The specification does not teach any other way of getting **an isolated nucleic acid** other than saying it could be screened using SEQ ID NO:1 or 3 sequence. Therefore, one skilled in art has to screen a large quantity of clinical samples from liver or pancreatic tissue of patients having HCC or pancreatic adenocarinoma to get **an isolated nucleic acid**. The specification does not teach any other **an isolated nucleic acid** except SEQ ID NO:1 or 3 that meets the functional description.

In summary, making **an isolated nucleic acid** before "[i]n determining whether **an isolated nucleic acid** falls within the scope of claim 1, requires undue experimentation because the only way to make **an isolated nucleic acid** other than SEQ ID NO:1 or 3 is to screen a large quantity of clinical samples from liver or pancreatic tissue of patients having HCC or pancreatic adenocarinoma. It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for themselves.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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March 14, 2004

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